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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,190	10/28/2003	Lloyd Wolfinbarger JR.	067949-5019-01	3910

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EXAMINER	
FORD, ALLISON M	
ART UNIT	PAPER NUMBER
1653	
MAIL DATE	DELIVERY MODE
01/06/2012	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/694,190	WOLFINBARGER ET AL.	
	Examiner	Art Unit	
	ALLISON FORD	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,3-7,9-12,16,19-21,23-27,29-33,39-46 and 68-74* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,3-7,9-12,16,19-21,23-27,29-33,39-46 and 68-74* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 6/11/2010 has been entered.

Priority

Acknowledgement is made of applicants claim for priority under 35 USC 120 as a continuation-in-part to prior filed application 09/660,422 (filed 12 September 2000), now US Patent 6,743,574.

Response to Arguments/Amendments

Applicants' arguments submitted 5/12/2009 have been fully considered, in combination with the amendments. Arguments pertaining to maintained rejections will be addressed below, as appropriate. Rejections/objections not repeated herein have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The amendments to the claims have obviated the previous grounds of rejection made under 35 USC 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Applicants have traversed the rejections under 35 USC 103(a) on the grounds that the Wolfinbarger, Jr et al (US Patent 6,024,735) only qualifies as prior art under 35 USC 102(e); Applicants have submitted a statement attesting that US Patent 6,024,735 and the present application were, at the time of the invention of the present application, were commonly owned by Lifenet Health. Applicants assert this is sufficient to disqualify US Patent 6,024,735 as prior art pursuant to 35 USC 103(c).

Applicants arguments have been fully considered, but are not found persuasive. It is respectfully submitted that Wolfinbarger, Jr (US Patent 6,024,735) was published on Feb. 15, 2000, and the inventors include only L. Wolfinbarger, Jr. The instant application has priority claims which extend to Sep. 12, 2000, and the inventors include L. Wolfinbarger, Jr, P. Lange, A. Linthurst, E. Moore, and B. Nolf. Thus Wolfinbarger, Jr et al (US Patent 6,024,735) was published less than one year before the effective filing date of the instant application and has a different inventive entity (i.e. 'by another'), making it available as prior art under 35 USC 102(a). The 103(c) exclusion will only disqualify prior art which was available under 35 USC 102(e), (f) or (g) (see MPEP 2146). An obviousness rejection based on a 102(a) reference can only be overcome by persuasively arguing a *prima facie* case of obviousness has not been established, amending the claims to overcome the rejection, or swearing behind the date of the reference by filing an affidavit or declaration under 37 CFR 1.131 (See MPEP 2141.01). Therefore, the rejection previously of record is still proper.

However, in order to facilitate compact prosecution, the rejections have been modified so as to rely on US Patent 5,797,871 (also to Wolfinbarger, Jr), which was published Aug 25, 1998, thus making it available as prior art under 35 USC 102(b).

Claims 1, 3, 4, 12, 16, 19-21, 23-27, 29-33, 39-46 and 68-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atala (US Patent 6,376,244), in light of the RPMI 1640 recipe (Joslin.org Website), and in view of Wolfinbarger, Jr (US Patent 5,797,871).

Atala disclose a process for decellularizing soft tissue organs for subsequent implantation into a mammalian system.

The method of Atala comprises mechanically agitating an isolated organ to disrupt cell membranes;

treating the mechanically agitated, isolated organ in a solubilizing fluid to extract cellular material from the organ (which Applicants call "extracting a soft tissue sample with an extracting solution") to produce an extracted organ;

washing the extracted organ in a washing fluid to remove cellular debris, to produce a substantially decellularized organ; and optionally

equilibrating the substantially decellularized organ in equilibrating fluid (which reads on a storing step) (See Atala, col. 2, ln 43-67).

Atala states the solubilizing fluid (which is considered to read on the extracting solution of the current claims) may be an alkaline solution having a detergent. A variety of detergents are disclosed, including sodium cholate and deoxycholates (See Atala, col. 3, ln 14-30). Sodium cholate and deoxycholate are cholic acid and deoxycholic acid in alkaline solution, and thus read on non-denaturing anionic detergents as defined by the instant invention. In Example 1 Atala carry out the solubilization (extraction) step at a temperature of 4°C (See Atala, col. 9, ln 55-65). Following extraction the tissue is

moved from the solubilizing fluid to the washing fluid; this step is considered to read on 'removing said non-denaturing anionic detergent.'

Atala states the washing fluid may be distilled water (See Atala, col. 3, ln 31-34).

Atala state the equilibrating solution (considered to read on the storage solution of the current claims) may comprise distilled water, physiological buffer and culture media (See Atala, col. 2, ln 64-67). Physiological buffer and culture media are considered to read on water replacement agents, as they are disclosed along with distilled water as suitable solutions which may be used. Since physiological buffer and/or culture medium can be used as alternatives to distilled water, they are thus appropriately considered 'water replacement agents.' It is further submitted that amongst the culture mediums which may be used as the equilibrating solution (storage solution) disclosed by Atala is RPMI 1640 medium (See Atala, col. 7, ln 51-58, referencing list of buffers and culture media disclosed at col. 6, ln 3-22); RPMI 1640 medium comprises glucose, proline, hydroxyproline, and i-inositol (a polyol), each of which are listed as water replacement agents in claim 21 (See RPMI 1640 Recipe).

It is noted that the method of Atala is reported to *substantially* decellularize the organ (See Atala, col. 2, ln 59-63 & claim 1); as such it is a reasonable interpretation that at least some cell lysis remnants remain in the final product. These cell lysis remnants are considered to read on "cellular elements capable of inducing graft repopulation with an appropriate cell type" as required by the instant inventions.

The method of Atala differs from the method of the current claims in that they do not teach including a decontaminating agents in the solubilizing (extracting) solution or in the storage solution. However, Wolfinbarger, Jr teach including decontaminating agents in detergent solutions intended to remove cellular lysis remnants from tissues and in storage solutions for storing decellularized tissues intended for subsequent use in implantation procedures to improve sterility (See Wolfinbarger, Jr, col. 8, ln 27-37). The decontaminating agent may be one or more of antibiotics, antiviral agents, hydrogen

peroxide, alcohols, such as methyl, ethyl, propyl, isopropyl, butyl, t-butyl, and sodium hydroxide (See Wolfinbarger, Jr. *id*). It is submitted that appropriate decontaminating agents and appropriate concentrations thereof would have been routinely optimized by one of ordinary skill in the art based on the tissue source and the level of suspected contamination. The obviousness of optimization of the concentrations is based on the legal precedent established in *In re Aller* which held that differences in concentration will not support patentability unless there is evidence that the claimed concentration is critical. See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Selection of different combinations of decontaminating agents for use in various steps throughout the method (i.e. use of one decontaminating agent in the extracting step, and use of a different decontaminating agent in the storage step) or use of a single decontaminating agent in multiple steps of the method (i.e. use of the same decontaminating agent in both the extracting step and the storage step) would have been routinely selected based on experimental design. Use of various combinations of decontaminating agents in different steps would provide the benefit of disinfecting multiple types of contaminants; use of a single type of decontaminating agent would simply the method and reduce the number of different reagents required to carry out the method. Thus, both methods have recognized benefits, but generally would have been expected to yield the predictable result of successfully decontaminating the tissue, overall. Thus, selection of either a combination of multiple types of decontaminating agents, or use of a single agent throughout, would have been *prima facie* obvious.

It is further noted, to improve sterility and reduce contamination, Wolfinbarger, Jr suggest use of endotoxin-free, deionized/distilled water (See Wolfinbarger, Jr col. 7, ln 59-63). One of ordinary skill in the art would have recognized the desirability of using USP grade, ultrapure, endotoxin free water for applications wherein the product is intended for implantation into mammalian systems, and thus use of such water would have been *prima facie* obvious in the method of Atala.

Some of the parameters and conditions required by the instant claims are not specifically disclosed by Atala or Wolfinbarger, Jr, specifically the concentration/amount of the detergent used in the solubilizing (extracting) fluid of Atala, the duration of the solubilizing (extracting) step, or the temperature at which the solubilizing (extraction) is to be carried out; however each of these parameters are recognized as result effective variables that directly affect the degree to which the organ is decellularized, and the extent to which the native structure of the matrix is retained. As result effective variables, each of these parameters would have been routinely optimized by one of ordinary skill in the art at the time the invention was made. "[W]here the general conditions of a claim are disclosed by the prior art it is not inventive to discover the optimum or workable ranges by routine experimentation" See *In re Aller* (supra).

With regards to the conditions under which the solubilizing (extracting) step is carried out, Atala states the concentration of detergent in the solubilizing fluid is a result effective variable, and would be varied based on the tissue being treated (See Atala, col. 6, ln 48-58 & col. 7, ln 18-31). The concentration of a particular detergent would be routinely optimized by one of ordinary skill in the art in order to achieve the desired result of effectively removing cellular components, without disrupting the interstitial structure of the organ, optimization would be based on the detergent and the tissue to be treated. It logically follows that the duration of the solubilization step (extracting step) would be recognized as a result effective variable that, too, would have been routinely optimized by one of ordinary skill in the art at the time the invention was made in order to achieve the desired result.

Optimization of the temperature is held to be *prima facie* obvious, this holding is based on legal precedent established in *In re Aller* (cited supra), that differences in temperature will not support patentability unless there is evidence that the claimed temperature is critical.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 3-7, 9-12, 16, 19-21, 23-27, 29-33, 39-46 and 68-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atala (US Patent 6,376,244), in light of the RPMI 1640 recipe (Joslin.org website), in view of Wolfinbarger, Jr (US Patent 5,797,871), and further in view of Wolfinbarger, Jr (US Patent 6,432,712).

The teachings of Atala and Wolfinbarger, Jr ('871) have been set forth in detail above. Neither Atala nor Wolfinbarger, Jr ('871) disclose including an endonuclease in the solubilizing (extracting) solution. However, Wolfinbarger, Jr ('712) discloses using a broad spectrum, recombinant endonuclease BENZONASE™ to decellularize organs and tissues (See Wolfinbarger, Jr ('712), col. 8, ln 40-67). Because the method of Atala is intended to result in a decellularized organ, it would have been *prima facie* obvious to one of ordinary skill in the art to include BENZONASE™ in the solution intended to remove cellular components from the organ. One would have had a reasonable expectation of successfully including BENZONASE, and determining an appropriate concentration, based on the teachings of Wolfinbarger, Jr ('712). (claims 5-7 and 9-11).

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting: Non-Statutory Obviousness-type

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided

the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Applicants have traversed the obviousness-type double patenting rejection over US Patent 6,734,018 on the grounds that "the '018 patent is no longer an issue with respect to obviousness double-patenting as the claim amendments render moot this rejection." Applicants have not specifically pointed out how the amendments obviate the rejection of record.

However, noting that claim 1 now requires a first decontaminating agent to be present in the extraction solution, and noting that the ‘018 patent does not include a decontaminating agent in the extraction solution, and that the '018 claims are limited by the closed language “consisting of” it is agreed that it would *not* have been obvious to modify the method of the ‘018 patent to further include a decontaminating agent in with the extraction solution. However, current claim 72 does not require the presence of a decontaminating agent within the extraction solution, but rather only requires the decontaminating agent in the storage solution. For the reasons discussed below, the patented claims are held to render obvious instant claim 72 and dependents thereof.

Claims 3, 4, 12, 16, 21, 23, 26, 27, 29-33, 40, 42, 44, 46, 68, and 72-are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10, 12-14, 19, 20, 23-34 and 41 of U.S. Patent No. 6,734,018 (hereafter "the '018 Patent").

The '018 patent claims a process for preparing an acellular soft tissue graft for implantation into a mammalian system, consisting of:

(a)inducing a pressure mediated flow of an extracting solution comprising one or more nonionic detergents and one or more endonucleases, through soft tissue, to produce extracted tissue;

(b) inducing a pressure mediated flow of a treating solution comprising one or more anionic detergents through said extracted tissue, to produce a treated tissue;

(c) inducing a pressure mediated flow of a decontaminating solution comprising one or more decontaminating agents through said treated tissue, to produce said acellular soft tissue graft; and

(d) storing said acellular soft tissue graft in a storage solution comprising one or more decontaminating agents. (Patented claim 10)

Noting the instant claims use the open transitional language 'comprising', the claimed method permits additional steps (such as the initial extracting step (a) of the '018 patent), as such, the method of the '018 patent is considered to render obvious the instantly claimed method as follows:

In the '018 patent step (b) of inducing a pressure mediated flow of a treating solution comprising one or more anionic detergents through the tissue is considered to read on the claimed method step of extracting the soft tissue with a non-denaturing anionic detergent to produce an extracted tissue. Claims 23-29 of the '018 patent define the anionic detergent as being identical to that used in the instant method, both in composition and concentration; thus the effect on the soft tissue is inherently the same.

In the '018 patent step (c) of inducing a pressure mediated flow of a decontaminating solution comprising one or more decontaminating agents through said treated tissue is considered to read on the claimed method steps of washing at least some cell lysis remnants from the extracted tissue with water. Claim 41 of the '018 patent explicitly requires a washing step with said decontaminating solution. Please note that patented claim 29 defines the decontaminating solution as comprising ultrapure, endotoxin-free water; please note that there is no requirement in the instant claims that excludes additional agents, such as decontaminating agents, from being further provided to the washing solution; thus patented step (c) involves washing the tissue with a solution comprising ultrapure, endotoxin-free water.

In the '018 patent step (c) of inducing a pressure mediated flow of a decontaminating solution comprising one or more decontaminating agents through said treated (and optionally washed) tissue is considered to further read on the claimed method step of inducing a pressure mediated flow of storage solution comprising a water replacement agent. Claim 32 of the '018 patent defines the decontaminating agents as including glycerol; glycerol is amongst those agents listed as a water replacement agent.

Finally, in the '018 patent step (d) of storing said acellular graft in a storage solution comprising at least one decontaminating agent reads on the claimed method step of storing the acellular tissue in a storage solution. Again the storage solution in the '018 patent can include ultrapure endotoxin free water (See '018 claim 30) and further comprise decontaminating agents such as antimicrobial agents chlorine dioxide, ethanol, methanol, isopropanol and glycerol (See '018 claim 31-33. It is further submitted that appropriate decontaminating agents and appropriate concentrations thereof would have been routinely optimized by one of ordinary skill in the art based on the tissue source and the level of suspected contamination. The obviousness of optimization of the concentrations is based on the legal precedent established in *In re Aller* which held that differences in concentration will not support patentability unless there is evidence that the claimed concentration is critical. See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Thus the method of the patented claims renders obvious instant claims 3, 4, 12, 16, 21, 23, 26, 27, 29-33, 40, 42, 44, 46, 68, and 72-74 (noting that independent claim 72 does not require the decontaminating agent in the extracting solution, but only in the storage solution).

Therefore the prior patent renders the instant claims *prima facie* obvious.

Applicants have traversed the obviousness-type double patenting rejection over US Patent 7,338,757, in view of US Patent 6,024,735, on the grounds that US Patent 6,024,735 does not qualify as prior art to the presently claimed invention, and that the claimed invention is not obvious in view of US Patent 7,338,757.

In response, Applicants' arguments have been fully considered, but are not found persuasive. As discussed above US Patent 6,024,735 *is* properly applied as art under 35 USC 102(a), however, for simplicity the rejection has been amended to rely on Wolfinbarger, Jr (US Patent 5,797,871).

Claims 1, 3, 4, 12, 16, 19-21, 23-27, 29-33, 39-46 and 68-74 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6-10, 13-15, 22

and 23 of U.S. Patent No. 7,338,757 (hereafter "the '757 Patent") in view of Wolfinbarger, Jr (US Patent 5,797,871; hereafter "Wolfinbarger, Jr").

The '757 patent claims a process for preparing an acellular soft tissue graft comprising:

(a) extracting at least one soft tissue sample with a buffered alkaline extraction solution which contains at least one nonionic detergent and at least one endonuclease, and which is hypotonic to the cells in said soft tissue sample,

(b) washing said extracted tissue in a first washing solution comprising water to produce a first washed tissue,

(c) treating said first washed tissue with a first processing solution comprising an anionic detergent to produce a first processed tissue,

(d) washing said first processed tissue in a second washing solution comprising water to produce a second washed tissue, and

(e) storing said second washed tissue in a storage solution comprising at least one decontaminating agent and water.

Noting the instant claims use the open transitional language 'comprising', the claimed method permits additional steps (such as the initial extracting step (a) of the '757 patent), as such, the method of the '757 patent is considered to render obvious the instantly claimed method. The '757 patent does not utilize a denaturing detergent (noting both nonionic and anionic detergents are non-denaturing) (relevant to instant claim 3)

In the '757 patent step (c) of treating the washed tissue with the first processing solution comprising an anionic detergent is considered to read on the claimed method step of extracting the soft tissue with a non-denaturing anionic detergent to produce an extracted tissue. Claims 6-9 of the '757 patent define the anionic detergent as being identical to that used in the instant method, both in composition and concentration; thus the effect on the soft tissue is inherently the same.

In the '757 patent step (d) of washing the first processed tissue in a washing solution comprising water is considered to read on the claimed method step of washing at least some remaining cell lysis remnants from the extracted tissue with water. It is noted that the '757 patent does not define the water as USP grade, endotoxin-free, deionized/distilled water, however, it is submitted that it would have been *prima facie* obvious to one of ordinary skill in the art to use USP grade, endotoxin-free, deionized/distilled water, as such water is routinely used in the art in processes relating to biological matter where sterility and contamination are a concern (see, e.g. Wolfinbarger, Jr col. 7, ln 59-63).

Finally, in the '757 patent step (e) of storing the washed tissue in a storage solution comprising at least one decontaminating agent clearly renders obvious the claimed method step of storing the washed tissue in storage solution comprising decontaminating agents. Claims 14 and 15 of the '757 patent define the decontaminating agent as an antimicrobial agent, such as chlorine dioxide, ethanol, methanol, or glycerol. Glycerol, at least, is also considered to read on a water replacement agent present in the storage solution. It is further submitted that appropriate decontaminating agents and appropriate concentrations thereof would have been routinely optimized by one of ordinary skill in the art based on the tissue source and the level of suspected contamination. The obviousness of optimization of the concentrations is based on the legal precedent established in *In re Aller* which held that differences in concentration will not support patentability unless there is evidence that the claimed concentration is critical. See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Therefore the prior patent renders the instant claims *prima facie* obvious.

The provisional rejection over Application 12/475,217 is withdrawn due to abandonment of the '217 application.

Claims 1, 3-7, 9-12, 16, 19-21, 23-27, 29-33, 39-46 and 68-74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, and 7-25 of copending Application No. 12/901,135. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the two applications is substantially the same. The same treatment steps with the same solutions are applied to tissues to decellularize and sterilize the tissues to produce devitalized soft tissue grafts which retain at least one non-viable cell or cellular element capable of inducing graft repopulation with an appropriate cell type.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALLISON FORD whose telephone number is (571)272-2936. The examiner can normally be reached on 10:00-7:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sue Liu can be reached on 571-272-5539. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Allison M. Ford/
Primary Examiner, Art Unit 1653